

Primary Prevention of Type 2 Diabetes Mellitus by Lifestyle Intervention: Implications for Health Policy

Centers for Disease Control and Prevention Primary Prevention Working Group*

More than 18 million Americans currently have diabetes mellitus. The economic and human cost of the disease is devastating. In the United States, diabetes is the most common cause of blindness among working-age adults, the most common cause of nontraumatic amputations and end-stage renal disease, and the sixth most common cause of death. For the cohort of Americans born in 2000, the estimated lifetime risk for diabetes is more than 1 in 3. In the next 50 years, the number of diagnosed cases of diabetes is predicted to increase by 165% in the United States, with the largest relative increases seen among African Americans, American Indians, Alaska Natives, Asian and Pacific Islanders, and Hispanic/Latino persons. Compelling scientific evidence indicates that lifestyle change prevents or delays the occurrence of type 2 diabetes in high-risk groups. This body of evidence from randomized, con-

trolled trials conducted in 3 countries has definitively established that maintenance of modest weight loss through diet and physical activity reduces the incidence of type 2 diabetes in high-risk persons by about 40% to 60% over 3 to 4 years. The number of persons at high risk for type 2 diabetes is similar to the number of persons who have diabetes. This paper summarizes scientific evidence supporting lifestyle intervention to prevent type 2 diabetes and discusses major policy challenges to broad implementation of lifestyle intervention in the health system.

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There are entirely too many diabetic patients in the country. Statistics for the last thirty years show so great an increase in the number that, unless this were in part explained by a better recognition of the disease, the outlook for the future would be startling.

—Elliott P. Joslin

More than 80 years have passed since Elliott P. Joslin wrote these words, appealing for a national effort in the United States to prevent diabetes mellitus (1). During the past 8 decades, however, the prevalence of diabetes has not decreased; instead, Joslin's vision of the future has become reality. Today, about 6.3% of the U.S. population—more than 18 million Americans—has diabetes (2). Type 2 diabetes accounts for 90% to 95% of all cases, which is probably a much higher proportion than in Joslin's time. The annual cost of the disease is estimated to be at least \$132 billion, more than 10% of U.S. expenditures on health care services (2, 3). Diabetes mellitus is the most common cause of blindness among working-age adults, the most common cause of nontraumatic amputations and end-stage renal disease, and the sixth most common cause of death in the United States (2). For the cohort of Americans born in 2000, the estimated lifetime risks for diabetes are 32.8% in men and 38.5% in women (4).

In the next 50 years, diagnosed diabetes is predicted to increase by 165% in the United States, with the largest relative increases seen among African Americans, American Indians, Alaska Natives, Asian and Pacific Islanders, and Hispanic/Latino persons (5). However, the greatest increases in diabetes are projected to occur in India, China, Pakistan, and Indonesia: By 2025, each of these countries is expected to have larger increases than the United States in the number of persons with diabetes (6).

Compelling scientific evidence exists that lifestyle

change prevents or delays the occurrence of type 2 diabetes. This body of evidence, obtained from 3 independent randomized, controlled trials from 3 countries (7–9), has definitively established that maintenance of modest weight loss (3 to 5 kg [7 to 10 lb]) through sustained lifestyle interventions that include diet and physical activity reduces the incidence of type 2 diabetes in high-risk persons by 40% to 60% over 3 to 4 years. However, few adults succeed in achieving and maintaining lower body weight; instead, continuing weight gain during much of adulthood is the norm (10). Furthermore, the current health system in the United States is not prepared to deliver lifestyle intervention.

We summarize the scientific evidence supporting lifestyle intervention to prevent type 2 diabetes, and we delineate 4 policy areas that present challenges for implementation in clinical practice: identification of candidates for diabetes prevention, delivery of lifestyle intervention, economics, and ethics.

CURRENT EVIDENCE FOR PRIMARY PREVENTION

In the past 3 decades, several clinical trials have tested lifestyle interventions and medications to prevent type 2 diabetes. In all trials, participants have had impaired glucose tolerance, on the basis of 2 blood glucose measurements: a fasting value less than 7.0 mmol/L (<126 mg/dL) and a value of 7.8 to less than 11.1 mmol/L (140 to <200 mg/dL) 2 hours after consumption of 75 g of glucose (11). Persons with impaired glucose tolerance are at substantially increased risk for type 2 diabetes (12).

Two decades ago, 3 small randomized, controlled trials of primary prevention of type 2 diabetes were performed in England (13, 14) and Sweden (15). The English trials found no effect of diet or oral medication. In the Swedish trial, the incidence of diabetes was reduced in persons who re-

Table 1. Summary of 3 Large Randomized, Controlled Clinical Trials of Primary Prevention of Type 2 Diabetes

| Variable | Da Qing IGT and Diabetes Study (7) | Finnish Diabetes Prevention Study (8) | Diabetes Prevention Program (9) |
|---|--|---|--|
| Participants, <i>n</i> | 520 | 522 | 3234 |
| Women, % | 47 | 67 | 68 |
| Mean age \pm SD, <i>y</i> | 45.0 \pm 9.1 | 55 \pm 7 | 50.6 \pm 10.7 |
| Mean body mass index \pm SD, <i>kg/m</i> ² | 25.8 \pm 3.8 | 31.2 \pm 4.6 | 34.0 \pm 6.7 |
| Race/ethnicity, % | | | |
| White | — | — | 55 |
| African-American, Hispanic, American Indian, and Asian | — | — | 45 |
| Study duration, <i>y</i> | 6 | 3.2* | 2.8* |
| Study groups | Control, diet, exercise, diet plus exercise | Control, lifestyle (weight loss, diet, physical activity) | Placebo, metformin, lifestyle (weight loss, physical activity, diet) |
| Adjusted reduction in the incidence of diabetes, % | Diet: 31 Exercise: 46 Diet plus exercise: 42 | Lifestyle: 58 | Metformin: 31 Lifestyle: 58 |

* Mean value.

ceived dietary counseling and tolbutamide; however, the data were not analyzed on an intention-to-treat basis.

In 1997, results were published from a 6-year randomized, controlled trial in which 33 clinics (557 persons with impaired glucose tolerance) in Da Qing, China, were randomly allocated to 1 of 4 study conditions: control, diet, exercise, or diet plus exercise (7). Compared with the control group, the incidence of diabetes was reduced in the 3 intervention groups by 31%, 46%, and 42%, respectively, although weight loss was modest. Possible limitations of the study findings included the randomization of clinics rather than persons and the fact that participants were leaner and lived in a different environment compared with their western counterparts (16).

In 2001, results were published from the Finnish Diabetes Prevention Study, a 3-year randomized, controlled trial of 522 obese persons with impaired glucose tolerance. Participants were randomly allocated on an individual basis to a control group or a lifestyle intervention group that emphasized physical activity, weight loss, limited total dietary intake and intake of saturated fat, and increased intake of dietary fiber. After the first year, the lifestyle intervention group had lost 3.4 kg more than the controls; at the end of the second year, the net weight loss was 2.7 kg in the lifestyle group. During the trial, the incidence of diabetes was reduced by 58% in the lifestyle group compared with the control group. Concerns were raised about the relevance of the findings to the culturally and ethnically heterogeneous U.S. population (16).

Most recently, the U.S. Diabetes Prevention Program (9) demonstrated the efficacy of lifestyle intervention to prevent type 2 diabetes. This program, which is the largest trial of primary prevention of diabetes to date, was conducted at 27 clinical centers. More than 3000 overweight and obese participants with impaired glucose tolerance were randomly allocated to 1 of 3 study conditions: control, use of metformin, or intensive lifestyle intervention. The goal of lifestyle intervention was to achieve and main-

tain 7% or greater weight loss through a low-calorie, low-fat diet and 150 or more minutes of moderate physical activity weekly (9). Nearly half the participants were African American, Hispanic American, Asian American, or Native American. Over 3 years, weight loss in the placebo, metformin, and lifestyle intervention groups averaged 0.1 kg, 2.1 kg, and 5.6 kg, respectively. The incidence of diabetes was reduced by 31% in the metformin group and 58% in the lifestyle group; the latter value is identical to that observed in the Finnish study. To prevent 1 case of diabetes, only 7 patients needed to be "treated" with lifestyle change, compared with 14 patients treated with metformin. The magnitude of risk reduction in the lifestyle intervention group was similar across all ethnic groups, and participants in all age and body mass index subgroups achieved a clinically significant reduction in risk. In contrast, metformin was relatively ineffective in older and less obese participants.

Implementation of this compelling evidence (Table 1) poses major policy challenges for public health and clinical medicine.

HOW SHOULD WE IDENTIFY CANDIDATES FOR PRIMARY PREVENTION?

The key eligibility criteria for the Diabetes Prevention Program included age 25 years or older, body mass index of 24 kg/m² or greater (≥ 22 kg/m² for Asian Americans), and impaired glucose tolerance plus an elevated fasting glucose level (5.3 to 6.9 mmol/L [95 to 125 mg/dL]) (9). Thus, if we extrapolate strictly from these criteria, diabetes prevention should focus on adults with these 3 characteristics. However, no efficacy studies exist for primary prevention of type 2 diabetes in normoglycemic obese persons, lean persons, children, or persons with impaired fasting glucose (fasting glucose level, 5.6 to <7.0 mmol/L [100 to <126 mg/dL]) (17) but not glucose intolerance. In 2002, the American Diabetes Association recommended

that all overweight people (body mass index ≥ 25 kg/m²) 45 years of age or older who have prediabetes (impaired glucose tolerance or impaired fasting glucose) should be considered potential candidates for diabetes prevention (18).

The number of persons in the United States who meet the criteria of the American Diabetes Association for prediabetes is unknown. The last nationally representative survey of the U.S. population assessed by oral glucose tolerance testing was the Third National Health and Nutrition Examination Survey, which was conducted from 1988 to 1994 and tested only adults 40 to 74 years of age (19). On the basis of data from that study, Benjamin and colleagues (20) estimated that 11.9 million overweight adults 45 to 74 years of age in the United States would meet the American Diabetes Association criteria in 2000 (17). Because the cut-point for impaired fasting glucose was recently decreased from 6.1 to 5.6 mmol/L (110 to 100 mg/dL) (17), this estimate is low. If data on glucose tolerance were available on the remaining adults 25 to 39 years and those older than 74 years, the total number of persons with prediabetes would probably approach the 18.2 million who are currently estimated to have diabetes (2). Saydah and colleagues estimated that 10 million Americans meet the criteria of the Diabetes Prevention Program for intervention (21). By any definition, the number of persons at high risk is substantial.

It is unclear how best to identify persons at high risk for diabetes. Use of the oral glucose tolerance test is inconvenient and time-consuming. No diabetes prevention trial has been conducted in persons with impaired fasting glucose, but about 24% of persons with prediabetes have impaired fasting glucose, and their demographic and cardiovascular risk factors are generally similar to those of persons with impaired glucose tolerance (20). Data are even more limited on the relationship between positive and negative results on nonfasting tests and subsequent classification by glucose tolerance testing (22, 23).

Candidates for primary prevention might be identified in the clinical care system at an "opportunistic" encounter: that is, during a visit by patients to their health care provider for a condition unrelated to diabetes prevention. This option is attractive because in 2000, 72.2% of U.S. adults reported they had visited a physician for a routine checkup in the previous year (24). Opportunistic screening has important limitations, however: Persons with limited or no access to clinical care will be missed and those with health insurance, those with access to higher-quality health care, and those who are more likely to use the health care system will be preferentially identified.

The U.S. Preventive Services Task Force concluded that evidence was insufficient to recommend for or against routine screening of asymptomatic adults for type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance but noted that intensive lifestyle intervention should be considered for patients with the latter 2 conditions (25). The recommendation of the Task Force is consistent with

that of American Diabetes Association: Opportunistic screening should be considered in persons 45 years of age or older, particularly those with a body mass index of 25 kg/m² or greater, and in younger overweight adults with another risk factor for type 2 diabetes (17).

Other settings offer opportunities for screening and identification. For example, public health agencies and community-based organizations may wish to conduct screening and identification efforts outside the clinical setting, such as mass screening programs in the general population. Such efforts would identify persons who may benefit from primary prevention. However, such programs have a responsibility to ensure medical follow-up of all participants with a positive result on a screening test. How will population-wide screening programs ensure that persons with positive results are referred and receive indicated clinical care, including appropriate diagnostic tests, and, if prediabetes is diagnosed, receive access to primary prevention interventions? The additional responsibility of ensuring clinical follow-up poses a substantial challenge.

The same challenge also applies to persons in whom diabetes is diagnosed as a result of screening, because these persons also require appropriate treatment. Analysis of data from the Third National Health and Nutrition Examination Survey indicates that screening for prediabetes could also identify some of the 6.5 million persons 45 to 74 years of age with previously undiagnosed diabetes (20). The total number of overweight adults in the United States who are 45 to 74 years of age and have prediabetes or undiagnosed diabetes is estimated to be 18.6 million (20). The challenge to an already stretched health system is formidable.

The difficult challenges facing opportunistic and population-wide screening for prediabetes raise the question of whether the blood glucose criterion should be eliminated. The idea of broadening eligibility for lifestyle intervention is appealing. First, the lifestyle intervention of the Diabetes Prevention Program is consistent with current recommendations for the general public on diet, nutrition, and physical activity (26). Second, the epidemic of overweight and obesity that is thought to be largely responsible for the diabetes epidemic has affected all segments of the U.S. population. Finally, lifestyle changes could have substantial collateral benefits, including decreased blood pressure, improved blood lipid levels, and better health-related quality of life (27, 28). Thus, is focusing intervention on only persons with prediabetes an adequate public health response? Why not move beyond the strong evidence from efficacy studies?

Reflecting the steady increase in overweight and obesity that has occurred over the past 20 years, 61% of U.S. adults 20 to 74 years of age were overweight or obese in 1999; indeed, 27% of all U.S. adults were obese (29). Another approach might target the 47 million Americans who meet the criteria for the metabolic syndrome (30). Given budgetary realities, provision of lifestyle intervention on this scale would probably substantially reduce the in-

tensity and effectiveness of the intervention. In addition, many people in this large pool will have normal glucose tolerance and may never develop diabetes. If eligibility for primary prevention of type 2 diabetes were broadened, these factors would need to be considered in order not to overwhelm the ability of the health care system to effectively prevent type 2 diabetes and to prevent and control complications in persons with diabetes.

HOW SHOULD LIFESTYLE INTERVENTIONS BE DELIVERED?

Although lifestyle interventions have great appeal, prescription medications are the intervention of choice in current practice: Sixty percent of visits to a physician's office result in a prescription being written (31). However, adherence to drug therapy for chronic health conditions is poor (32), adverse effects of medication errors are too common (33), and prescription drugs contribute strongly to the escalating cost of health care (34). Pharmaceutical interventions for chronic health conditions are appealing and straightforward. In contrast, even the most highly motivated physicians typically have minimal education or training in lifestyle intervention, and they usually have inadequate access in their practice to the resources needed to support lifestyle intervention. Well-intentioned attempts by physicians to practice "lifestyle medicine" with scarce resources can lead to embittered rejection of health promotion (35).

Primary prevention of type 2 diabetes raises several issues related to integration of lifestyle intervention in clinical practice. Although the specific interventions vary, all involve dietary change and increased physical activity to achieve weight loss (Table 1). A fundamental issue is the appropriate role of physicians. No efficacy study (7–9) had physicians directly involved in delivering interventions, but physicians did provide clinical oversight during the intervention process, working with intervention staff and providing encouragement to patients.

Integration of lifestyle intervention into current health care systems will require that physicians have ready access to effective programs and providers of lifestyle intervention, perhaps within the physician's own institution or at commercial firms that provide lifestyle programs by referral. Wherever interventions are provided, they must be linked to the community, its culture, and its values (36). Currently, it is unknown whether other practicing professionals could deliver interventions in the community with efficacy similar to that of the interventionists of the Diabetes Prevention Program, who were trained in counseling on nutrition, exercise, and behavior modification (9). A new category of health interventionist may be needed, in substantial numbers, to deliver and sustain lifestyle intervention in the large number of persons who would be eligible for these services. Who will be responsible for administration of lifestyle intervention, how will quality be assessed and ensured, and how will society pay for these

services and this new class of provider? Dietitians (37), diabetes educators (38), health educators, nurses, and community health workers are leading candidates. Efforts are under way to define clinical roles and responsibilities for facilitating adherence to lifestyle change (39). A detailed description of the proven lifestyle intervention developed by the Diabetes Prevention Program has been published (40).

Despite strong supporting evidence, the premise that lifestyle intervention should be integrated into clinical medicine has been questioned (41). In one scenario, a meaningful decrease in diabetes will be achieved only by changing the underlying environmental factors that contribute to obesity and sedentary behaviors in the general population. Furthermore, because lifestyle interventions delivered within the health care system are assumed to be expensive and the groups at greatest risk for diabetes are least able to negotiate their "obesogenic" environments, lifestyle intervention will inevitably fail (41). In comparison, the cost of effective environmental solutions for diabetes prevention is said to be "trivial" (41). Although environmental approaches, such as pedestrian-friendly community design and improved access to healthy food choices, could support change in the general population, little evidence is available on cost or effectiveness (42). Changes at multiple levels will probably be needed to sustain lifestyle intervention.

WHAT ARE THE ECONOMIC IMPLICATIONS?

Lifestyle intervention is often assumed to be too expensive for the health care system (41). However, few careful economic evaluations of diabetes prevention have been published (43).

Economic studies must answer 2 key questions about an intervention: How much does it cost, and is it a good value? To be useful for policymakers, both questions should be answered from the perspectives of payers and society (44). From the payer perspective (for example, a health insurer), only the direct medical costs of the intervention are relevant, because these are the costs for which the payer must reimburse the health care system. Direct medical costs include the costs of delivering the intervention, the costs of treating adverse effects of the intervention, and any cost savings that may occur from improved health status of those receiving the intervention (for example, reduction in hospital days and in use of prescription medications). From the societal perspective, additional costs are important. These include patient-specific direct medical costs (such as deductibles and copayments), direct nonmedical costs (such as out-of-pocket costs to purchase exercise equipment and cost of participant time to exercise), and indirect costs (such as cost of time lost from work because of injury while exercising).

The Diabetes Prevention Program is unique in including a prospective economic evaluation in its study design. Data have been systematically collected on direct medical

costs, direct nonmedical costs, and indirect costs (45). Economic evaluation of the Diabetes Prevention Program allows the cost, and the cost-effectiveness, of lifestyle intervention and metformin therapy to be directly compared from both the payer and societal perspectives. From the perspective of a health system, the total cost per participant of metformin therapy and lifestyle interventions at 3 years were \$2191 and \$2269, respectively, compared with the placebo group (46). From the perspective of society, costs were \$2412 and \$3540 per participant (46), indicating that both interventions had modest incremental costs.

The full health benefits of preventing type 2 diabetes are not likely to emerge during the relatively short time frame of a clinical trial because collateral health benefits may also improve future health status. Additional economic evaluations are needed to examine the longer-term effect of diabetes prevention, including analyses that use mathematical models to estimate potential future reductions in microvascular and macrovascular complications of diabetes and associated costs of maintaining lifestyle change (47).

Within-trial economic evaluations of diabetes prevention also need to be supplemented with cost studies performed in real-world clinical and public health settings. Additional factors may affect the cost and effectiveness of lifestyle intervention, including geographic location; patient age, sex, ethnicity, education level, and socioeconomic status; and structural and reimbursement policies of different health care organizations. Empirical studies will be important to determine the economic consequences of alternative approaches to identify persons eligible for primary prevention interventions.

WHAT ARE THE ETHICAL IMPLICATIONS?

Different perspectives exist on the putative benefits of health promotion programs directed to disease prevention, such as weight loss to prevent type 2 diabetes. Some assert that health promotion activities should be widely applied because the results are obviously beneficial with no substantial adverse effect (48), whereas others describe health promotion as inherently “tyrannical” (49, 50). The thinking of most health professionals probably falls between these two extremes. What are the ethical implications of translating diabetes prevention by lifestyle intervention into clinical practice?

Possible harm associated with health recommendations has recently received considerable attention, especially medical errors (33). Do broad, population-based programs require less evidence of efficacy than do individual clinical interventions (48)? An opposing view holds that an even greater proof is necessary in population-wide health promotion than in clinical care because of constraints on personal liberty and autonomy (51). Evidence that health promotion aimed at the general public will improve health needs to be even stronger than evidence for treating sick patients (51, 52).

Although efficacy studies, such as the Diabetes Prevention Program, are an essential step in improving health, they may not affect medical practice because of the “translation gap” (53). This effect may reflect ethical tension between the high internal validity, and often low “generalizability,” of clinical trials. All of the major efficacy studies of lifestyle for primary prevention of diabetes were restricted to persons with glucose intolerance, who are at very high risk for type 2 diabetes. Strong internal validity is desirable in an efficacy study, to establish causation. Lifestyle intervention can indeed prevent the development of type 2 diabetes in persons at high risk. However, the effectiveness of lifestyle intervention for persons at lower risk for diabetes is unknown. Is it ethical to await results of a new, extensive series of randomized controlled trials to evaluate intervention efficacy in groups at lower risk for diabetes? Or is it acceptable to infer intervention efficacy in groups other than those defined by the eligibility criteria of the Diabetes Prevention Program?

Despite high interest on the part of the public and media in lifestyle approaches and support from respected authorities, the public is becoming overburdened with health recommendations, many of which are unclear, inconsistent, and impractical (42). Disease prevention programs that do not work in the real world, even if grounded in science, may erode public confidence in lifestyle change as a worthy goal.

A third source of potential harm from broad-based disease prevention programs relates to the concepts of “limits” and “opportunity cost,” that is, the opportunity forgone by spending fixed resources on one program instead of another (54, 55). In medicine, as in all endeavors, available resources, including time, personnel, knowledge, and money, are limited. Strong scientific and economic evidence supports the benefits of secondary and tertiary prevention of complications of diabetes, and although gaps exist in clinical practice, the situation is improving (56). Implementation of lifestyle programs for primary prevention of diabetes without full consideration of the effect on resources needed for other proven, effective diabetes treatment programs could set back efforts to reduce the overall burden of diabetes.

Completion of a landmark study such as the Diabetes Prevention Program represents a major milestone in prevention of chronic disease. Health professionals must ensure that the ethical mandate of nonmaleficence, *primum non nocere*—first, do no harm—applies to health promotion and disease prevention programs as well as to clinical medicine.

SUMMARY

The scientific evidence supporting primary prevention of diabetes by lifestyle intervention is compelling. However, the promise of achieving primary prevention of diabetes by lifestyle intervention must be accompanied by careful consideration of health policy issues (Table 2).

Table 2. Key Policy Issues Related to Primary Prevention of Type 2 Diabetes by Lifestyle Intervention*

| Policy Area | Potential Options |
|--|--|
| Identification of persons for lifestyle intervention | Only persons meeting DPP criteria Persons with glucose intolerance Persons with impaired fasting glucose Persons with metabolic syndrome Overweight persons Persons with family history of diabetes General population |
| Lifestyle interventions in the health care system | Physicians deliver intervention Ancillary staff delivers intervention, with physician oversight Outside firm delivers intervention, with physician oversight Environmental change at population level to change lifestyle, outside the health care system |
| Economics | Interventions fully reimbursed by insurance Patients pay part or all costs out-of-pocket Taxes used for environmental change with no reimbursement for clinical intervention |
| Ethics | Conduct efficacy studies in other risk groups Intervene in groups similar to DPP risk group, use process information for later decision to broaden population served Begin funding primary prevention Fund only after understanding effect on diabetes treatment programs Identify persons with prediabetes before assurance of availability of lifestyle interventions Identify persons with prediabetes only if lifestyle intervention is available Begin public information campaign on lifestyle intervention Develop a consistent, science-based message among key federal agencies, health care providers, and payers before beginning public information program |

* DPP = Diabetes Prevention Program.

Many key research questions to inform policy development exist. What are the most effective and efficient approaches to identify subgroups and individuals for lifestyle intervention? What are the best methods of achieving and sustaining lifestyle change throughout the lifespan? What changes to the health system and policy are needed to support and sustain lifestyle intervention? And, what are the appropriate roles and responsibilities of the physician, the health care system, and public health in primary prevention? Economic analyses are essential to inform policymaking, particularly to quantify the absolute costs and the value of lifestyle and other competing interventions. Finally, development of public policy will require an open and thoughtful discussion to address, if not resolve, the ethical challenges of integrating lifestyle intervention for primary prevention into the health care system.

These policy challenges are occurring on a background of chronic limitations in resources and an ever-increasing

burden of type 2 diabetes and its complications in the population. As more Americans develop type 2 diabetes during middle age rather than later in life, they will spend increasing periods of time living with the devastating complications of the disease. This adds considerable urgency to public policy deliberations on the matter. Effective implementation of primary prevention of type 2 diabetes represents a unique opportunity to reduce the burden of diabetes and its complications. Such implementation also carries with it a major responsibility for continued clinical and public health action in secondary and tertiary prevention, some 80 years after Joslin's prescient observations.

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APPENDIX

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